Contents

1 Estrogens, Adiposity and the Menopause ....................... 1

2 The Link Between Obesity and Breast Cancer Risk: Epidemiological Evidence ................................... 5
  2.1 BMI and Breast Cancer Risk ................................ 5
  2.2 BMI and Breast Tumor Hormone Receptor Status........ 7
  2.3 Obesity and Mammographic Density ..................... 8
  2.4 Waist-to-Hip Ratio and Breast Cancer ................... 8
  2.5 The Metabolic Syndrome, Diabetes Mellitus and Breast Cancer .............................................. 9
  2.6 Breast Size and Breast Cancer ........................... 10
  2.7 Effect of Obesity on Disease-Free Survival ............ 10

3 Adipose-Derived and Obesity-Related Factors and Breast Cancer ............................................. 11
  3.1 Adipokines .................................................. 11
  3.2 Inflammatory Factors ..................................... 12
  3.3 Insulin and Insulin-Like Growth Factor-1 (IGF-1) .... 14
  3.4 Estrogens .................................................... 14

4 Estrogen Biosynthesis ........................................... 17
  4.1 Source of Estrogens in Pre-versus Postmenopausal Women 17
  4.2 The Aromatase Enzyme .................................... 17
  4.3 Local Aromatase Expression in Breast Cancer .......... 19
  4.4 The CYP19A1 Gene and Tissue-Specific Expression ... 21
  4.5 Promoter-Specific Regulation of Aromatase in Obesity and Breast Cancer .............................. 23
    4.5.1 Prostaglandin E₂ ....................................... 26
    4.5.2 Leptin ..................................................... 32
    4.5.3 Adiponectin .............................................. 33
    4.5.4 IL-6 ......................................................... 33
    4.5.5 TNFα ....................................................... 33
    4.5.6 Insulin and IGF-1 ....................................... 34
    4.5.7 Other Tumor-Derived Factors ............................ 35
5 Therapy Aimed at Breaking the Linkage Between Obesity and Breast Cancer

5.1 Effect of Obesity on Endocrine Therapy Efficacy

5.2 Targeting Obesity-Related Estrogen Biosynthesis

5.2.1 Weight Loss, Exercise and Bariatric Surgery: Effect on Breast Cancer Risk and Estrogen Levels

5.2.2 Insulin Sensitizers and Anti-diabetics

5.2.3 Other Targeted Therapies

Conclusions

References
Obesity and Breast Cancer
The Role of Dysregulated Estrogen Metabolism
Brown, K.A.; Simpson, E.R.
2014, IX, 56 p. 9 illus., 7 illus. in color., Softcover
ISBN: 978-1-4899-8001-4